Researchers develop new cells meant to form blood vessels, treat peripheral artery disease

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Researchers have developed a technique to jump-start the body's systems for creating blood vessels, opening the door for potential new treatments for diseases whose impacts include amputation and blindness.

The international team, led by scientists at the Indiana University School of Medicine, is targeting new therapies for illnesses such as peripheral artery disease, a painful leg condition caused by poor blood circulation. The disease can lead to skin problems, gangrene and sometimes amputation.

While the body has cells that specialize in repairing blood vessels and creating new ones, called endothelial colony-forming cells, these cells can lose their ability to proliferate into new blood vessels as patients age or develop diseases like peripheral arterial disease, said Mervin C. Yoder Jr., M.D., Richard and Pauline Klingler Professor of Pediatrics at IU and leader of the research team.

Peripheral artery disease patients can be given medication to improve blood flow, but if the blood vessels to carry that improved flow are reduced in number or function, the benefits are minimal. If "younger," more "enthusiastic" endothelial colony forming cells could be injected into the affected tissues, they might jump-start the process of creating new blood vessels. Gathering those cells would not be easy however—they are relatively difficult to find in adults, especially in those with peripheral arterial disease. However, they are present in large numbers in umbilical cord blood.

Reporting their work in the journal *Nature Biotechnology*, the researchers said they had developed a potential therapy through the use of patient-specific induced pluripotent stem cells, which are normal adult cells that have been "coaxed" via laboratory techniques into reverting into the more primitive stem cells that can produce most types of bodily tissue. So, in one of the significant discoveries reported in the *Nature Biotechnology* paper, the research team developed a novel methodology to mature the induced pluripotent stem cells into cells with the characteristics of the endothelial colony-forming cells that are found in umbilical cord blood. Those laboratory-created endothelial colony-forming cells were injected into mice, where they were able to proliferate into human blood vessels and restore blood flow to damaged tissues in mouse retinas and limbs.

Overcoming another hurdle that has been faced by scientists in the field, the research team found that the cord-blood-like endothelial colony-forming cells grown in laboratory tissue culture expanded dramatically, creating 100 million new cells for each original cell in a little less than three months.

"This is one of the first studies using induced pluripotent stem cells that has been able to produce new cells in clinically relevant numbers—enough to enable a clinical trial," Dr. Yoder said. The next steps, he said, include reaching an agreement with a facility approved to produce cells for use in human testing. In addition to peripheral artery disease, the researchers are evaluating the potential uses of the derived cells to treat diseases of the eye and lungs that involve blood flow problems.

More information: Differentiation of human pluripotent stem cells to cells similar to cord-blood endothelial colony–forming cells, *Nature Biotechnology*, DOI: 10.1038/nbt.3048

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